Citation:

Yaari S, Goldbourt U. Voluntary and involuntary weight loss: Associations with long-term mortality in 9,228 middle-aged and elderly men. *American Journal of Epidemiology*. 1998; 148: 546-555.

PubMed ID: 9753009

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine if weight loss among men between 40 to 65 years of age over a five-year period is associated with increased risk of all-cause mortality.

Inclusion Criteria:

- There does not appear to be any specific inclusion/exclusion criteria for this study
- All study participants were examined in 1963 and prevalence of any diseases or disorders was noted. Patients were then followed and re-examined in 1968. I would need to go back to the original published study to determine this.

Exclusion Criteria:

- There does not appear to be any specific inclusion/exclusion criteria for this study
- All study participants were examined in 1963 and prevalence of any diseases or disorders was noted. Patients were then followed and re-examined in 1968.

Description of Study Protocol:

Recruitment

Participants in this study were recruited to participate in the Israeli Ischemic Heart Disease Study. Further details have been published previously.

Design

- A prospective follow-up cohort study of 10,059 men between 40 and 65 years of age in 1963, when they were first examined or recruited to participate in the study

- At the first examination in 1963, weight and height was measured in 10,034 men
- Of these participants, 9,228 survivors participated in the 1968 examination and were included in the analysis.

Dietary Intake/Dietary Assessment Methodology

- Participants were required to complete a questionnaire in 1963
- Based on their responses they were then categorized into groups based on if they reported they were on a diet to lose weight, on a diet for health reasons or not on a diet.

Statistical Analysis

- All-cause mortality and cause-specific mortality rates per 1,000 person years were calculated for the following five weight change ranges:
    - Extreme weight loss (5kg or more)
    - Modest weight loss (2 to 4kg)
    - Stable weight (-1kg)
    - Modest weight gain (2 to 4kg)
    - Extreme weight gain (5kg or more)
- The Cochran-Mantel-Haenszel method was used to estimate the pooled risk of coronary heart disease (CHD) mortality and all-cause mortality in men with extreme weight loss (between 1963 and 1968) compared to men who kept their weight stable during this time period. Results were stratified into five age groups:
    - 40 to 49 years of age
    - 50 to 59 years of age
    - 60 to 69 years of age
    - 70 to 79 years of age
    - 80 or more years of age
- Cox's life table proportional hazards model was used to perform multivariate analysis of mortality:
    - Adjusted relative risk (RR) and 95% CI were estimated for all-cause and CHD mortality for each of the five weight-change ranges
    - The model included: Age, smoking status, BMI, serum total cholesterol, systolic blood pressure (SBP), prevalence of diabetes, cancer, angina pectoris, intermittent claudication and myocardial infarction (MI)
    - A dummy variable was introduced into the model if the patient reported being on a diet or not
    - Two alternative analysis conducted were:
        - An analysis that adjusted for the 1963 levels of all risk factors as well as prevalence of diseases or disorders and also accounted for possible confounding by the pre-weight change levels
        - Another analysis adjusted for the 1968 levels of the same variables and history of lung disease (diet information from 1963 was used in this analysis because this information was not collected in 1968)
        - All analyses were repeated after excluding deaths occurring during the first five years of follow-up (1968 to 1973) to eliminate a possible effect of pre-existing diseases on weight change and mortality)
- Kaplan-Meier and Cox-adjusted survival estimates were used to assess the effect of weight change (by weight change category) on survival (calculated and plotted with 18-year total mortality) and were adjusted for age and the other variables adjusted for in the other statistical tests.

Data Collection Summary:

Timing of Measurements

- All study participants were initially examined in 1963. At that time, weight, height, blood pressure and serum total cholesterol were measured
- Patients with clinically recognized MI, CHD, diabetes mellitus, cancer, chronic lung disease or angina were also diagnosed or noted in 1963 upon examination and again in 1968 in 95% of living participants
- Participants completed a questionnaire in 1963 and reported whether or not they were on a diet to lose weight, for health reasons or not at all. This information was not collected again in 1968.

Dependent Variables

- *Variable 1:* Mortality (all-cause)
- *Variable 2:* Mortality (cause-specific).

Independent Variables

- *Variable 1:* Change in body weight (classified into five groups as noted above in the statistical section)
- *Variable 2:* Body mass index (BMI) (classified into five categories).

Control Variables

- Age
- Smoking status
- BMI
- Blood pressure
- Serum total cholesterol
- Prevalence of diabetes, cancer, angina pectoris, intermittent claudication and MI
- Diet.

Description of Actual Data Sample:

- *Initial N:* 10,059 men when they were first examined
- *Attrition (final N):* In 1963, weight and height were measured in 10,034 of the 10,059 participants. Of these participants, 9,228 survivors participated in the follow-up examination in 1968
- *Age:* 40 to 65 year old men (at the beginning of the study in 1963)
- *Ethnicity:* Israeli
- *Other relevant demographics:* Tenured civil servants and municipal employees
- *Anthropometrics:* Weight and BMI were measured at baseline and at follow-up. There do appear to be some differences between the groups when looking at the baseline data; however, it does not appear that a statistical comparison was done to determine if there were significant differences among baseline characteristics of participants.
- Loca*tion:* Israel.

Summary of Results:

Only men in the top BMI quintile had significantly increased long term mortality.

18-year Age-adjusted Mortality Rates per 1,000 Person-years by BMI Groups

Variables	BMI Group One	BMI Group Two	BMI Group Three	BMI Group Four	BMI Group Five
	<22kg/m^2	22 to 25kg/m^2	25 to 27kg/m^2	27 to 30kg/m^2	30kg/m^2 or more
Mortality	16.5	13.8	14.9	16.3	20.1

18-year Age-Adjusted Mortality Rates per 1000 person years and Relative Risk by Age Groups

Variables	Age Group One	Age Group Two	Age Group Three
	40 to 49 Years	50 to 59 Years	60 Years or More
Mortality rates among extreme losers	13.0	29.2	50.8
Mortality rates in stable weight group	9.4	21.1	42.3
Relative risk of mortality	1.38	1.55	1.20

18-year Age-Adjusted Mortality Rates per 1000 person years by Weight Change Groups: Overall and by Dieting Status

Variables	Weight Change Group One	Weight Change Group Two	Weight Change Group Three	Weight Change Group Four	Weight Change Group Five
	Extreme Weight Loss (5kg or More)	Modest Weight Loss (2 to 4kg)	Stable Weight (-1kg or Less Weight Change to 1kg or Less)	Modest Weight Gain (2 to 4kg)	Extreme Weight Gain (5kg or More)
Overall mortality rates	20.9	17.1	15.3	14.2	14.8
Mortality (excluded first five years of follow-up data)	18.7*	15.2*	13.3*	11.6*	11.0*

Mortality rates: On diet for medical reasons (N=1,835)	23.7	21.8	17.2	16.1	16.7
Mortality rates: On weight loss diet (N=636)	23.5	19.9	12.7	15.9	17.5
Mortality rates: Not on a diet (N=6,646)	10.9	15.4	14.9	13.4	14.1

*Analysis was conducted after exclusion of the first five years of follow-up (1968 to 1973) to eliminate a possible effect of pre-existing disease.

Relative Risk of Mortality Among Extreme Weight Losers Compared with Weight Maintainers Among All Age Groups

Variables	Total Mortality	CVD Mortality	Non-CVD Mortality	CHD Mortality	Cancer Mortality
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Mortality relative risk	1.36 (1.20 to 1.55)	1.40 (1.16 to 1.69)	1.33 (1.11 to 1.59)	1.55 (1.25 to 1.93)	0.09 (0.65 to 1.24)

Relative Risk of Mortality by Weight Change between 1963 and 1968*

Variables	Weight Change Group One	Weight Change Group Two	Weight Change Group Three	Weight Change Group Four	Weight Change Group Five
	Extreme Weight Loss (5kg or More) RR (95% CI)	Modest Weight Loss (2 to 4kg) R (95% CI)	Stable Weight (-1kg or Less Weight Change 1kg or Less) RR (95% CI)	Modest Weight Gain (2 to 4kg) R (95% CI)	Extreme Weight Gain (5kg or More) RR (95% CI)
All-cause mortality in 1963	1.18 (1.03 to 1.35)	1.04 (0.93 to 1.16)	1.00	0.93 (0.84 to 1.02)	0.98 (0.88 to 1.10)
All-cause mortality in 1968	1.24 (1.08 to 1.42)	1.06 (0.94 to 1.19)	1.00	0.90 (0.82 to 1.01)	0.91 (0.80 to 1.02)

CHD mortality in 1963	1.22 (0.97 to 1.53)	0.88 (0.72 to 1.07)	1.00	0.86 (0.72 to 1.02)	0.99 (0.81 to 1.22)
CHD mortality in 1968	1.42 (1.12 to 1.79)	0.95 (0.77 to 1.17)	1.00	0.84 (0.70 to 1.01)	0.86 (0.69 to 1.06)

*All analyses were adjusted for the following covariates: Age, BMI, SBP, serum total cholesterol, smoking, diabetes, cancer, history of MI, definite angina, intermittent claudication, history of chronic lung disease and being on a diet in 1963.

Author Conclusion:

- Weight reduction over a five-year period was associated with an increased risk of cardiovascular and non-cardiovascular mortality
- The results of this study did not show an association between weight loss and an increase in cancer mortality
- Participants who were leaner (BMI less than 22kg/m^2) at the beginning of the study and lost weight over the five-year period had an greater increase in mortality risk than participants with higher initial weights
- Overall, the results of this study indicate that weight loss among middle-aged and elderly men, voluntary or involuntary, may be associated with a small increase in the risk of all-cause mortality.

Reviewer Comments:

The authors addressed the study limitations well and acknowledged the need for further long-term studies to examine the recommendation of weight reduction as a preventive health measure.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	No
4.1.	Were follow-up methods described and the same for all groups?	Yes

4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	No
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes

7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	No
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	No
10.2.	Was the study free from apparent conflict of interest?	Yes